Non-human Primates: The Appropriate Subjects of Biomedical Research?

Quigley, Muireann

DOI:
10.1136/jme.2007.020784

Document Version
Peer reviewed version

Citation for published version (Harvard):
Quigley, M 2007, 'Non-human Primates: The Appropriate Subjects of Biomedical Research?', *Journal of Medical Ethics*, vol. 33, no. 11, pp. 655-8. https://doi.org/10.1136/jme.2007.020784

Non-human Primates: The Appropriate Subjects of Biomedical Research?*

Abstract

Following the publication of the Weatherall report (a report on the use of non-human primates in research) this paper reflects on how to provide appropriate and ethical research models for research that is to be of benefit to humankind. Two of the main arguments that are used as a justification for the use of non-human primates in biomedical research are analysed. These are the 'least harm greatest good' and capacity arguments. This paper argues that these are equally applicable when considering whether or not humans are the appropriate subjects of biomedical research.

DOI: http://dx.doi.org/10.1136/jme.2007.020784

Introduction

The recent publication of the Weatherall report (a report on the use of non-human primates in research) offers us an occasion to reflect on how to provide appropriate and ethical research models for research that is to be of benefit to humankind. The central goal of the working group which produced this report was to consider the scientific case for the use of non-human primates in medical research in this country.[1] The report concentrated its investigation on the major areas in which non-human primate research is currently taking place: infectious diseases and neuroscience. Within these it was noted that the majority of research takes place by the pharmaceutical industry for drug development and toxicology studies. Primates are superior to other animal models for this type of research because of their "similarities with human physiological and behavioural characteristics".[2]

Given that biomedical research as a whole, and research in communicable diseases and the neurosciences in particular, may reap vast benefits for humankind, saving lives and decreasing disease morbidity, then it is imperative that it is carried out. The question, however, is who or what are the appropriate subjects of such research. The Weatherall report deals solely with biomedical research as applied to non-human primates and, to that end, includes a commendable section on the ethics of the use of non-human primates for this. The issues discussed included, but were not restricted to, the moral status of non-human primates, cost-benefit analyses, personhood, sentience, and intelligence, and the conclusion reached was that:

> The justification for the continued use of non-human primates in research is that their use is required lest greater harm occur (p.130).[2]

* I would to thank the reviewers for their helpful comments.

The construction of these arguments produced by the Weatherall Committee appears to be both logically and ethically sound. However, it also appears that the key arguments used which indicate why this research should be carried out in non-human primates could also indicate why such research in fact ought to be carried out in human primates. If this is true, and I will argue in this paper that it is, then one comes to the inescapable conclusion that human rather than non-human primates are the appropriate subjects of this type of biomedical research.

The Least Harm and the Greatest Good

This justification cited above is based upon "the fact that the numbers of non-human primates used any medical experiment are very small and . . . the number of humans whose suffering is ameliorated is often very large" (p.130).[2] This is essentially a utilitarian argument involving the balancing of cost versus benefit. On this type of analysis, having taken into account the relative suffering of non-human primates versus human primates, and the relatively small numbers of non-human primates used versus the potentially huge benefit for a large number of humans, it does seem ethically justifiable to use non-human primates in medical research.

However, these arguments are not only robust arguments for the use of non-human primates in medical research, but are also very good arguments for indicating why such research in fact ought to be carried out in human primates. This type of utilitarian argumentation would not only endorse the use of a relatively small number of humans for use in medical research but would, in combination with scientific evidence, make the use of humans ethically preferable. Given that the scientific case for the use of non-human primates rests on their similarity to humans, the only scientifically better model would be *actual* humans. It might be argued that it is often easier to control for experimental variables within animal populations than within human populations. However, you are more likely to generate aberrant outcomes when experimenting on non-humans as opposed to humans. This is because no matter how much you control for external parameters there may be biological differences which cannot be controlled for. There may intra-human variation when experimenting on humans but essentially the physiology remains within fixed bounds. Additionally it is clear that we cannot derive final and conclusive results from animal and non-human primate experimentation; if we could there would be no phase I, II, or III clinical trials in humans. Given this then we must seriously consider the case for using a very small number of humans for the large number whose suffering would be ameliorated. What exactly this might entail will be discussed later in the paper.

This might be a contentious claim but if the use of humans in such research is not morally acceptable, whereas the use of non-human primates is, then we are committed to giving a robust reason why this is so. To decide that such a course of action is permissible by virtue of the non-human status of some primates alone cannot be considered to be justifiable. To do this would be tantamount to what Singer calls speciesism[3] and is

void of decent moral justification in the same way that sexism and racism are. We must, therefore, ask ourselves what the morally relevant differences are (if any) between humans and non-human primates (and indeed between the higher non-human primates and the lower ones) that would justify us treating them differently.

More Alike Than We Think

One way of doing this might be to look at the characteristics possessed by each that might have a bearing on their moral status. This is important because in trying to decide whether or not it is justifiable to carry out biomedical research on non-human primates rather than humans we need to decide if the non-human primates have a moral status equivalent to that of humans, a moral status that is less than that, or whether they are in fact of no moral concern to us at all.

The relevant characteristics, and the crux of this moral difference, according to the report seems to be "a difference in self-awareness, cognitive awareness, cognitive capacities and sentience between most non-human primates and most humans" (p.130).[2] This is a differentiation based on capacity, and again it looks like a strong argument for the use of non-human primates in biomedical research. As Rachels maintains:

> [I]nsofar as a human and a member of another species are similar, they should be treated similarly, while to the extent that they are different, they should be treated differently.[4]

This is a similar notion to what Singer means when he says that animal's deserve an "equal consideration".[5] It represents the fact that if one makes a moral judgement with respect to specific criteria for a human, then if an animal meets those same criteria it is entitled to an equivalent judgement.

In this respect, while being our closest relative on the evolutionary scale, the non-human primates do appear to have less self-awareness, cognitive awareness, and cognitive capacities than the normal adult human primates.[6] The problem, however, again becomes the fact that this type of reasoning is equally applicable to inter-human considerations as it is to those involving non-human primate versus human primate. Not all humans have equal capacities, and if it is justifiable to use capacity to differentiate between non-human primates and human primates, it is justifiable to use it to differentiate between humans themselves. Babies, young children, some severely disabled adults, and those in a permanent vegetative state (PVS) not only display less capacity than fully competent human adults but also display less than some non-human primates.

Of course we could decide that these characteristics are not relevant. However, if we are to disregard and ignore the similarities and differences in capacity held by non-human primates that might speak for their moral status, then in the interests of consistency we ought to disregard those same characteristics in humans as well. And were we to do that there could be no good reason not to experiment on those humans of a similar level of capacity to that of most non-human primates.

Humans, Primates, and International Guidelines

The numbers of non-human primates used in biomedical research as a whole is relatively small.[7] As pointed out above it is this fact, coupled with the benefit to a large number of people, which forms part of the justification for using them in this type of research. I made the case that this argument coupled with the scientific superiority of humans as the research model means that we ought to seriously consider the case for replacing the very small number of non-human primates with an equally small number of humans.

It is a fact that there are many more humans involved as subjects in biomedical research than there are non-human primates.[8] The majority of this research on humans is on fully competent adults who have consented to their participation, and most of this research could be quantified in terms of risk or invasiveness as mild to moderate. This would be research which might involve observational studies, studies where biological samples such as blood, studies involving minor surgery such as creating skin lesions, or toxicity studies for drugs. The inherent risks, however, are ones which the (presumably) rational and competent adults who do take part in medical research are willing to take.

Of those humans who do participate in biomedical research there is also a small proportion of them who lack capacity and who are, therefore, not legally competent to consent to their own involvement. We still permit the participation of such individuals as research subjects, but they are heavily protected by national and international research guidelines.[9] These guidelines have been developed with the express purpose of protecting those individuals whose lack of capacity makes them vulnerable. The International Ethical Guidelines for Biomedical Research produced by the Council for International Organizations of Medical Sciences (CIOMS) says that 'special justification' is needed for the participation of vulnerable individuals in research.[10] Included in the categories of vulnerable people are those with 'limited capacity'.[10] It seems to me that most non-human primates are of a level of capacity that, if they were human, would fall into this 'vulnerable persons' category, and would, therefore, have these guidelines speaking for their protection. Now if as argued previously we cannot differentiate between non-human primates and humans merely on the grounds of species membership, and if there is no difference in capacity between non-human primates and some humans, then surely these guidelines ought to protect both.

If this is so then such guidelines ought to be consistently applied. There is one particular provision of interest which appears in slightly different formulations in both the Declaration of Helsinki and the CIOMS guidelines and that is essentially that medical research on vulnerable individuals must be either of benefit to that individual directly or be of benefit to people of their kind. The Declaration of Helsinki states that:

> These groups should not be included in research unless the research is necessary to promote the health of the population

> represented and this research cannot instead be performed on legally competent persons.[11]

Similarly the CIOMS guidelines state that:

> [T]he research is intended to obtain knowledge that will lead to improved diagnosis, prevention or treatment of diseases or other health problems characteristic of, or unique to, the vulnerable class – either the actual subjects or other similarly situated members of the vulnerable class.[10]

It is difficult to see how the medical research carried out on non-human primates can ever be said to be of direct benefit to them or to their kind. At least research on vulnerable humans is of benefit to humankind. If we do want to concede that this research is of benefit to their kind then we must be their kind. And if we accept this as true we are another step closer to accepting that there does not appear to be a difference between human and non-human primates that justifies medical research on them but not us.

Severely Invasive research

The kind of research discussed above that humans do participate in, vulnerable or not, involves those procedures or studies which can be deemed to mild to moderately risky or invasive. The majority of research that is carried out on the non-human primates also falls into this category.[12] Fully competent adults already make decisions to participate in the majority research that carries this level of risk or invasiveness. For that reason there is at least the presumption that we could get such people to participate in all research of this manner. While it is probable that the difference in capacities experienced by non-human primates and adult humans means that there is a qualitative difference in the way they experience suffering, it is not clear that this directs us to using the non-human primates for such research. But whilst the competent adult human might experience some suffering they can at least understand and rationalise it. These reasons, combined with the fact that humans are the scientifically preferable models for research that is to be of benefit to humankind, mean that there can be no good moral reason why we ought to use primates for this type of research.

However, it is likely that we would be left with a small portion of biomedical research that no competent adult would consent to participate in. This is research that is of a highly invasive or risky nature; the type of research that the Weatherall Report maintains would be 'totally inappropriate' in humans (p.36).[2] Examples of this might be research that involves being infected with viral agents like HIV (pp.43-57),[2] or which requires producing experimental brain lesions (p.67).[2] What then are we to do in this situation? Are we simply not to conduct this type of research?

It may be that this is the right course of action, but if, as intimated in the Weatherall Report, the real dangers posed to individuals and to humankind by certain illnesses and diseases are so immense then we may be remiss in our moral duties if this research is not done. If this is the case

then such dangers coupled with the potential benefits to humankind from this type of research might constitute that 'special justification' required by the CIOMS guidelines for the participation of those 'vulnerable' individuals mentioned earlier. Of course, as also mentioned earlier, consistency would dictate that we include both 'vulnerable' human and non-human primates of limited capacity in this.[13]

This is not to say that I am putting forward a case for ascribing rights to non-human primates, or indeed to animals in general. I am not. But then neither am I advocating the ascription of rights to those humans of a similar level of capacity. If one thinks, as I do, that the normative function of rights is the protection of autonomy, then those which do not have the requisite capacity for autonomy cannot be rights-holders.[14] That said the moral supportability of our treatment of any being does not reside in rights. That they are not deemed to be rights-holders is not to say that either the 'vulnerable' human or non-human primates are outwith our sphere of moral concern.

Conclusion

It seems that the benchmark of whether or not it is morally justifiable to conduct certain types of medical research on non-human primates is whether or not we would carry out that research on humans of a similar level of capacity. If we decide that research on these types of humans is acceptable then it is celebration time for the non-human primates as they are no longer needed because the scientific evidence tells us that research on humans is better. If on the other hand we decide that research on this category of humans is not ethically acceptable then I can see no good reason why it ought to be conducted on non-human primates. Either way it seems that the non-human primates win.

References

1. There are many stages and facets of biomedical research and not all involve non-human primates or even humans. Stages of research include basic and applied research, *in vitro* research on cell and tissue cultures, and *in vivo* research in the form of pre-clinical animal trials and clinical trials in humans.

2. The report of Sir David Weatherall's working group, 'The use of non-human primates in research', p.60. In studying infectious diseases it is the differences in the immune systems between the non-human primates and other animals which render them better models, and in the neurosciences it is the similarity of their brain neural circuitry

3. Singer P. *Animal Liberation: A New Ethics for our Treatment of Animals.* New York: New York Review/Random House, 1975.

4. Rachels J. Darwin, Species and Morality *Monist* 1987; 70: 98-113, p.109.

5. Singer P. All Animals Are Equal in Regan T. and Singer P. (Eds.) *Animal Rights and Human obligations*. New Jersey: Prentice-Hall Inc., 1976, p.154.

6. See Gallup GGJ. Chimpanzees: Self-recognition *Science* 1970; 167: 86-87, Gallup GGJ. Anderson JR. Shillito DJ. In Beckoff M. Allen C. Burghardt GM. (Eds.) *The Cognitive Animal: Empirical and Theoretical Perspectives on Animal Cognition.* Cambridge, MA: MIT Press, 2002, Hauser MD. *Wild Minds: What Animals really Think.* New York: Owl Books, 2001, and Roth G. and Dicke U. Evolution of the Brain and Intelligence *Trends in Cognitive Science* 2005; 9: 250-257.

7. In the EU in 2002 10,362 non-human primates were used in experiments. Commission of the European Communities. *Fourth Report on the Statistics on the Number of Animals Used for Experimental and Other Scientific Purposes in the member States of the European Union* (2005). In the same year 52,279 were used in the USA. USDA, *Annual Report of Enforcement for the Fiscal Year 2002.* Riverdale: MD, 2003.

8. A quick look at only four clinical trials involving human participants verifies this. There have been four ISIS (International study of infarct survival) trials which have investigated the treatment of patients with acute myocardial infarction. These involved 16,027, 17,187, 41,299, and 58,050 participants respectively, a total of 132,563 participants. See Randomised trial of intravenous atenolol among 16027 cases of suspected acute myocardial infarction: ISIS-1. *Lancet* 1986; 2: 57-66, Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988; 2: 349-60, ISIS-3: a randomised comparison of streptokinase vs. tissue plasminogen activator vs. anistreplase and of aspirin plus heparin vs. aspirin alone among 41,299 cases of suspected acute myocardial infarction. *Lancet* 1992; 339: 753-770, and ISIS-4: A randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected myocardial infarction. *Lancet* 1995; 334: 669-84.

9. Some of these include the Council for International Organizations of Medical Sciences (CIOMS) Guidelines, the World medical Association Declaration of Helsinki (2000), the Oviedo Convention of the Council of Europe (Convention for the protection of Human Rights and dignity of the human being with regards to the application of biology and medicine: Convention on Human Rights and Biomedicine – ETS No.: 164), and Directive 2001/20.EC of the European Parliament and of the Council.

10. Guideline 13, The Council for International Organizations of Medical Sciences (CIOMS) Guidelines.

11. World Medical Association, Declaration of Helsinki, Section B(24)

12. Home Office *Statistics of Scientific Procedures on Living Animals Great Britain 2004.* London: HMSO, 2006.

13.There may be a capacity-based argument that would point to research on vulnerable humans being less desirable than that on non-human primates. This argument appeals not to the capacities of the vulnerable humans themselves but rather those of their nearest and dearest. It is likely that the use of these humans would generate suffering for those people who care for them. This might perhaps give us a reason not to use them in this manner.

14. For further discussions on rights in general see Jones P. *Rights.* Basingstoke: MacMillan, 1994; Raz J. On the Nature of Rights. *Mind* XCIII, 1984; Sumner L.W. *The Moral Foundation of Rights.* Oxford: Clarendon Press, 1987; and Waldron J. (Ed.). *Theories of Rights*. Oxford: Oxford University Press, 1984.